# STIC Search Report
## Biotech-Chem Library

## STIC Database Tracking Number: 114210

**TO: Cybille Delacroix**
**Location: REM4C70**
**Art Unit: 1614**
**Sunday, February 15, 2004**

**Case Serial Number: 10/038114**

**From: Mary Jane Ruhl**
**Location: Biotech-Chem Library**
**Remsen 1-B55**
**Phone: 571-272-2524**

**maryjane.ruhl@uspto.gov**

## Search Notes

Examiner Delacroix,

Here are the results for your recent search request.

Please feel free to contact me if you have any questions about these results.

Thank you for using STIC services. We appreciate the opportunity to serve you.

Sincerely,

Mary Jane Ruhl
Technical Information Specialist
STIC
CM-1, Rm. 6-A-06
605-1155

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

# SEARCH REQUEST FORM

114210 / 114385
Rem 4C85

Requestor's Name: Delacroix 7100 Serial Number: 10/038,114

Date: 2-11-04 Phone: 571-272-0573 Art Unit: 1614

**Search Topic:**

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search the attached compound in a method for decreasing intraocular pressure or improving ocular accommodation.

involves treating patients with glaucoma.

key terms -> reduced accommodation.

Thank you

RECEIVED
FEB 12 2004
TECH CENTER 1600/2900

**STAFF USE ONLY**

Date completed:
Searcher: _____
Terminal time: _____
Elapsed time: _____
CPU time: _____
Total time: _____
Number of Searches: _____
Number of Databases: _____

**Search Site**
_____ STIC
_____ CM-1
_____ Pre-S

**Type of Search**
_____ N.A. Sequence
_____ A.A. Sequence
_____ Structure
_____ Bibliographic

**Vendors**
_____ IG Suite
_____ STN
_____ Dialog
_____ APS
_____ Geninfo
_____ SDC
_____ DARC/Questel
_____ Other

```
=> d his ful

     FILE 'REGISTRY' ENTERED AT 18:47:46 ON 15 FEB 2004
                E 3-CARBAMOYL-1-(4-METHOXY-BENZYL)-PYRIDINIUM CHLORIDE/CN
L1              STR
L2            1 SEA SSS SAM L1

     FILE 'HCAPLUS' ENTERED AT 19:01:18 ON 15 FEB 2004
L3            1 SEA ABB=ON  L2
```

see d que stat, attached

I could locate only 1 compd., ~~and such~~ and it is not shown in CAS as the chloride. When I searched it in CA Plus, I retrieved only 1 citation which does not pertain to glaucoma. Inventor's search does not show the elected speacie.

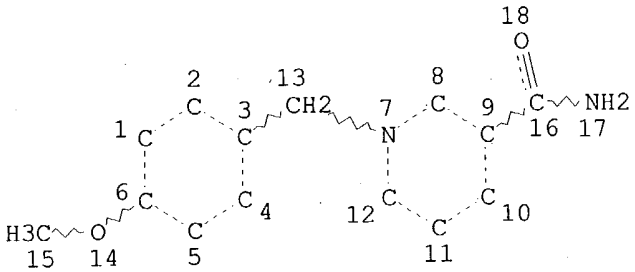
Pls. let me know if you need further work on this search.

Thank you,

Mary Jane Ruhl

x 22524

```
=> d que stat l3
L1                STR
```

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE
L2             1 SEA FILE=REGISTRY SSS SAM L1
L3             1 SEA FILE=HCAPLUS ABB=ON  L2
```

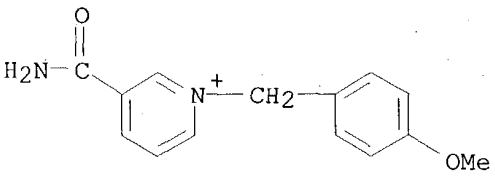
=> d ibib abs hitstr l3 1-1

L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:191937 HCAPLUS
DOCUMENT NUMBER: 124:316412
TITLE: Reactions of Charged Substrates. 4. The Gas-Phase Dissociation of (4-Substituted benzyl)dimethylsulfoniums and -pyridiniums
AUTHOR(S): Buckley, Neil; Maltby, David; Burlingame, Alma L.; Oppenheimer, Norman J.
CORPORATE SOURCE: School of Pharmacy, University of California, San Francisco, CA, 94143-0446, USA
SOURCE: Journal of Organic Chemistry (1996), 61(8), 2753-62
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relative rates for the gas-phase dissociation RX+ → R+ + X° of five (4-Y-substituted benzyl)dimethysulfoniums (Y = MeO, Me, H, Cl, and NO2) and 24 (4-Y-substituted benzyl)-3'-Z-pyridiniums (complete series for Z = CN, Cl, CONH2, and H, and 4-methoxy- and 4-nitrobenzyls for Z = F and CH3CO) were measured using liquid secondary ion mass spectrometry. The Hammett plot (vs δΔG0 or σ+) is linear for the sulfoniums, but plots for the four pyridinium series have a drastic break between the 4-Cl and 4-NO2 substrates. Broensted-like plots for the pyridiniums show a strong leaving group effect only for 4-nitrobenzyls. An anal. of these linear free energy relations with supporting evidence from semiempirical computations suggests that collisionally activated pyridinium substrates dissociate through two pathways, direct dissociation and an ion-neutral complex intermediate. Comparison of these results with results for the solution reactions of some of these compds. shows that the mechanism is different in the gas and solution phases. Sufficient exptl. data are not available to assign a mechanism for dissociation to the sulfonium series, but computational results show characteristics of a direct dissociative mechanism.

IT **175979-55-2**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(kinetics and mechanism of gas-phase dissociation of substituted benzyldimethylsulfoniums and -pyridiniums)

RN 175979-55-2 HCAPLUS
CN Pyridinium, 3-(aminocarbonyl)-1-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



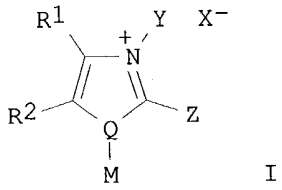
=> d ibib abs hitstr l11 1-2

L11 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:521491 HCAPLUS
DOCUMENT NUMBER: 137:78956
TITLE: Synthesis of thiazolium and imidazolium salts and use in treating **glaucoma**
INVENTOR(S): Egan, John J.; **Wagle, Dilip**; Vasan, Sara; **Gall, Martin**; **Bell, Stanley C.**; **Lavoie, Edmond J.**
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

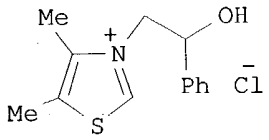
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002053158 | A1 | 20020711 | WO 2001-US49550 | 20011228 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1353669 | A1 | 20031022 | EP 2001-988353 | 20011228 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |

PRIORITY APPLN. INFO.:
US 2000-259426P P 20001229
US 2001-296257P P 20010606
US 2001-307418P P 20010724
WO 2001-US49550 W 20011228

OTHER SOURCE(S): MARPAT 137:78956
GI



I



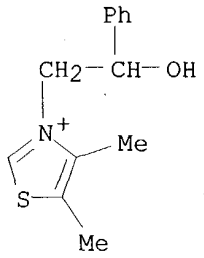
II

AB Provided is a method of decreasing intraocular pressure or improving ocular accommodation comprising administering I [R1-2 = H, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, etc.; Z = H, alkyl, Ar-CH2, NR3R4, etc.; R3-4 = H, alkyl, Ar, Ar-alkyl; Ar = (hetero)aryl; Y = amino, CHR5R6; R5 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aminoalkyl, etc.; R6 = H, alk(en/yn)yl, cyano, aryl/heterocycle, etc.; Q = N, O, S; M is absent when Q = O, S; M = alkyl, vinyl, allyl, Y; X = pharmaceutically acceptable anion]. Examples include, 11 compds., effect of example compds. on outflow facility primates, drug penetration

studies on intact cornea (rabbit, monkey), effect of compds. on i.m. pilocarpine-stimulated accommodative response (monkey) and the ability of test compds. to inhibit crosslinking (and reverse already formed cross linking) of glycated serum albumin to rat tail tendon collagen (which prevent outflow). For instance, 2-Chloro-1-phenylethanol (preparation given) was used to alkylate 4,5-dimethylthiazole (neat, 135°, 28 h) to afford II (9.7%) as prisms, mp 201-203°. I are useful in the treatment/prevention of **glaucoma.**

IT **356759-42-7P 356759-43-8P 356759-44-9P**
**356759-45-0P 356759-46-1P 356759-47-2P**
**356759-48-3P 356759-50-7P 356759-52-9P**
**356759-53-0P 392710-36-0P 392710-37-1P**
**392710-38-2P 393121-65-8P 393121-77-2P**
**393121-80-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**antiglaucoma** agent; synthesis of thiazolium and imidazolium salts as **antiglaucoma** agents)

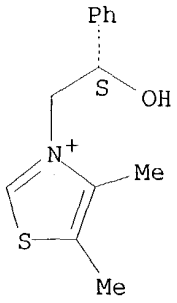
RN 356759-42-7 HCAPLUS
CN Thiazolium, 3-(2-hydroxy-2-phenylethyl)-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)




● Cl⁻

RN 356759-43-8 HCAPLUS
CN Thiazolium, 3-[(2S)-2-hydroxy-2-phenylethyl]-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)

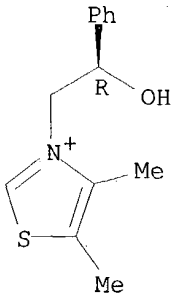
Absolute stereochemistry. Rotation (-).




● $Cl^-$

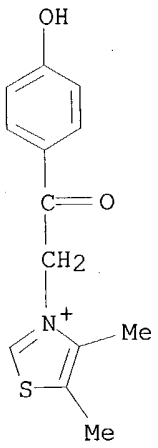
RN 356759-44-9 HCAPLUS
CN Thiazolium, 3-[(2R)-2-hydroxy-2-phenylethyl]-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



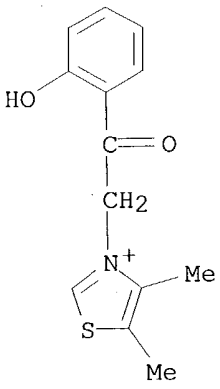

● $Cl^-$

RN 356759-45-0 HCAPLUS
CN Thiazolium, 3-[2-(4-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



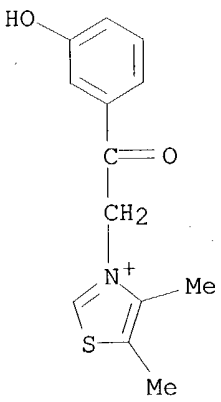

● $Br^-$

RN 356759-46-1 HCAPLUS
CN Thiazolium, 3-[2-(2-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



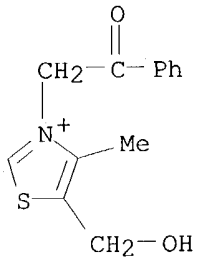

● $Br^-$

RN 356759-47-2 HCAPLUS
CN Thiazolium, 3-[2-(3-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



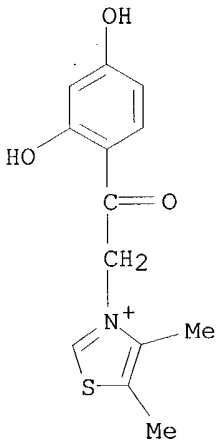
● $Br^-$

RN 356759-48-3 HCAPLUS
CN Thiazolium, 5-(hydroxymethyl)-4-methyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



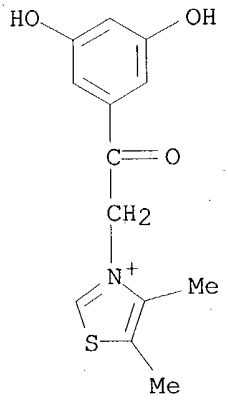
● $Cl^-$

RN 356759-50-7 HCAPLUS
CN Thiazolium, 3-[2-(2,4-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



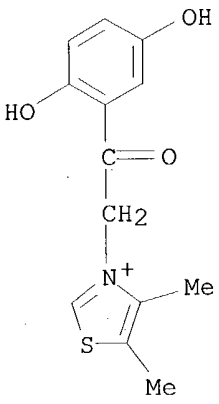
● $Br^-$

RN 356759-52-9 HCAPLUS
CN Thiazolium, 3-[2-(3,5-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



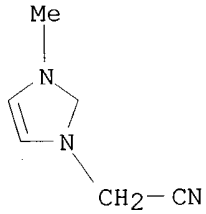
● $Br^-$

RN 356759-53-0 HCAPLUS
CN Thiazolium, 3-[2-(2,5-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



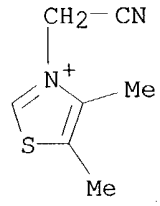
● $Br^-$

RN 392710-36-0 HCAPLUS
CN 1H-Imidazolium, 1-(cyanomethyl)-3-methyl-, bromide (9CI) (CA INDEX NAME)



● $Br^-$

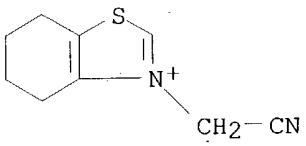
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 392710-37-1 HCAPLUS
CN Thiazolium, 3-(cyanomethyl)-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



● $Br^-$

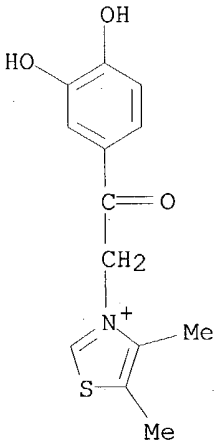
RN 392710-38-2 HCAPLUS

CN Benzothiazolium, 3-(cyanomethyl)-4,5,6,7-tetrahydro-, bromide (9CI) (CA INDEX NAME)



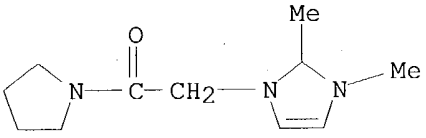
● $Br^-$

RN 393121-65-8 HCAPLUS
CN Thiazolium, 3-[2-(3,4-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)



● $Cl^-$

RN 393121-77-2 HCAPLUS
CN 1H-Imidazolium, 1,2-dimethyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, chloride (9CI) (CA INDEX NAME)

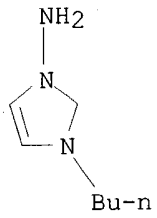


● $Cl^-$

*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 393121-80-7 HCAPLUS
CN 1H-Imidazolium, 1-amino-3-butyl-, salt with 2,4,6-trimethylbenzenesulfonic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

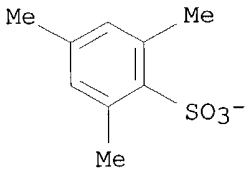
CRN 401514-28-1
CMF C7 H14 N3



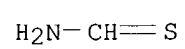

*** FRAGMENT DIAGRAM IS INCOMPLETE ***

CM 2

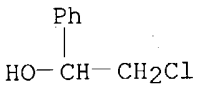
CRN 46149-61-5
CMF C9 H11 O3 S



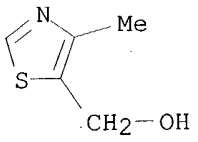

IT **115-08-2P**, Thioformamide **1674-30-2P**, 2-Chloro-1-phenylethanol **1977-06-6P**, 4-Methyl-5-(hydroxymethyl)thiazole **2491-36-3P 2491-37-4P 2491-38-5P 2491-39-6P 4433-49-2P 20266-00-6P**, N-(Chloroacetyl)pyrrolidine **20582-55-2P**, 4-Methyl-5-(ethoxycarbonyl)thiazole **25015-91-2P 56751-12-3P 62932-92-7P 70111-05-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; synthesis of thiazolium and imidazolium salts as **antiglaucoma** agents)
RN 115-08-2 HCAPLUS
CN Methanethioamide (9CI) (CA INDEX NAME)



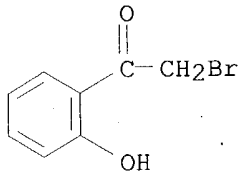

RN 1674-30-2 HCAPLUS
CN Benzenemethanol, α-(chloromethyl)- (9CI) (CA INDEX NAME)



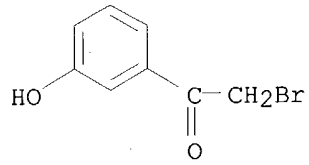
RN 1977-06-6 HCAPLUS
CN 5-Thiazolemethanol, 4-methyl- (8CI, 9CI) (CA INDEX NAME)



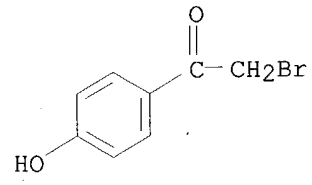
RN 2491-36-3 HCAPLUS
CN Ethanone, 2-bromo-1-(2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



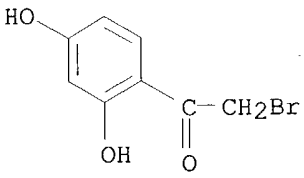
RN 2491-37-4 HCAPLUS
CN Ethanone, 2-bromo-1-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)



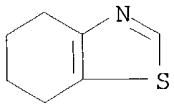
RN 2491-38-5 HCAPLUS
CN Ethanone, 2-bromo-1-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



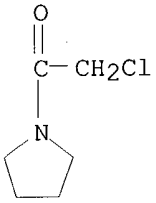
RN 2491-39-6 HCAPLUS
CN Ethanone, 2-bromo-1-(2,4-dihydroxyphenyl)- (9CI) (CA INDEX NAME)



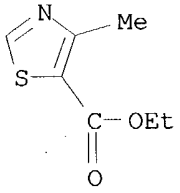
RN 4433-49-2 HCAPLUS
CN Benzothiazole, 4,5,6,7-tetrahydro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



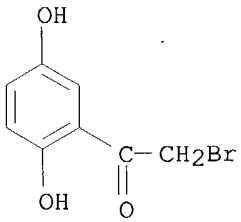
RN 20266-00-6 HCAPLUS
CN Pyrrolidine, 1-(chloroacetyl)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 20582-55-2 HCAPLUS
CN 5-Thiazolecarboxylic acid, 4-methyl-, ethyl ester (6CI, 8CI, 9CI) (CA INDEX NAME)

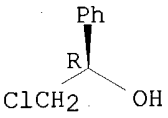


RN 25015-91-2 HCAPLUS
CN Ethanone, 2-bromo-1-(2,5-dihydroxyphenyl)- (9CI) (CA INDEX NAME)

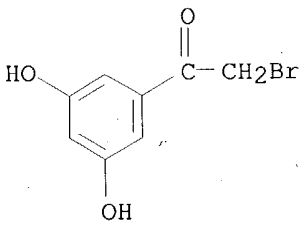


RN 56751-12-3 HCAPLUS
CN Benzenemethanol, α-(chloromethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

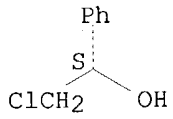


RN 62932-92-7 HCAPLUS
CN Ethanone, 2-bromo-1-(3,5-dihydroxyphenyl)- (9CI) (CA INDEX NAME)



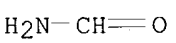
RN 70111-05-6 HCAPLUS
CN Benzenemethanol, α-(chloromethyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



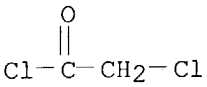
IT **75-12-7**, Formamide, reactions **79-04-9**, Chloroacetyl chloride **89-84-9 99-40-1 99-93-4**, 4-Hydroxyphenylethanone **118-93-4**, 2-Hydroxyphenylethanone **121-71-1**, 3-Hydroxyphenylethanone **123-75-1**, Pyrrolidine, reactions **490-78-8 532-27-4**, 2-Chloroacetophenone **590-17-0**, Bromoacetonitrile **609-15-4**, Ethyl 2-chloroacetoacetate **616-47-7**, 1-Methylimidazole **822-87-7**, 2-Chlorocyclohexan-1-one **1739-84-0**, 1,2-Dimethylimidazole **3581-91-7**, 4,5-Dimethylthiazole **4316-42-1**, 1-Butylimidazole **36016-40-7**, O-Mesitylene sulfonylhydroxylamine **51863-60-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; synthesis of thiazolium and imidazolium salts as **antiglaucoma** agents)

RN 75-12-7 HCAPLUS
CN Formamide (8CI, 9CI) (CA INDEX NAME)

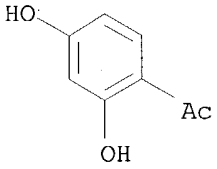


RN 79-04-9 HCAPLUS

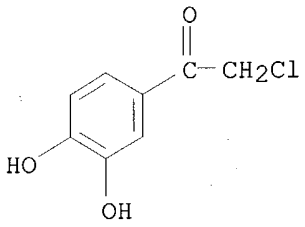
CN Acetyl chloride, chloro- (6CI, 8CI, 9CI) (CA INDEX NAME)



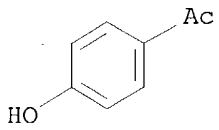
RN 89-84-9 HCAPLUS
CN Ethanone, 1-(2,4-dihydroxyphenyl)- (9CI) (CA INDEX NAME)



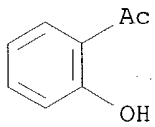
RN 99-40-1 HCAPLUS
CN Ethanone, 2-chloro-1-(3,4-dihydroxyphenyl)- (9CI) (CA INDEX NAME)



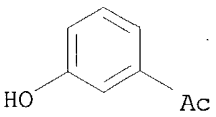
RN 99-93-4 HCAPLUS
CN Ethanone, 1-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



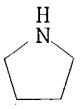
RN 118-93-4 HCAPLUS
CN Ethanone, 1-(2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



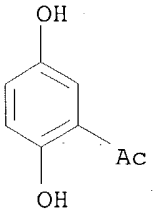
RN 121-71-1 HCAPLUS
CN Ethanone, 1-(3-hydroxyphenyl)- (9CI) (CA INDEX NAME)



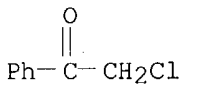
RN 123-75-1 HCAPLUS
CN Pyrrolidine (8CI, 9CI) (CA INDEX NAME)



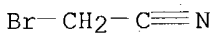
RN 490-78-8 HCAPLUS
CN Ethanone, 1-(2,5-dihydroxyphenyl)- (9CI) (CA INDEX NAME)



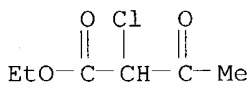
RN 532-27-4 HCAPLUS
CN Ethanone, 2-chloro-1-phenyl- (9CI) (CA INDEX NAME)



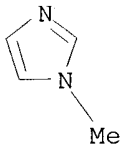
RN 590-17-0 HCAPLUS
CN Acetonitrile, bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



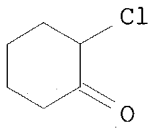
RN 609-15-4 HCAPLUS
CN Butanoic acid, 2-chloro-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)



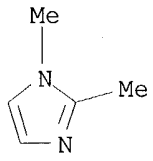
RN 616-47-7 HCAPLUS
CN 1H-Imidazole, 1-methyl- (9CI) (CA INDEX NAME)



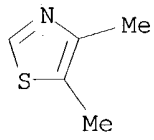
RN 822-87-7 HCAPLUS
CN Cyclohexanone, 2-chloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



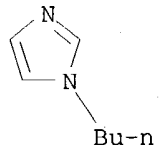
RN 1739-84-0 HCAPLUS
CN 1H-Imidazole, 1,2-dimethyl- (9CI) (CA INDEX NAME)



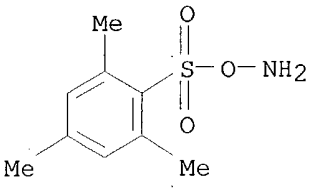
RN 3581-91-7 HCAPLUS
CN Thiazole, 4,5-dimethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



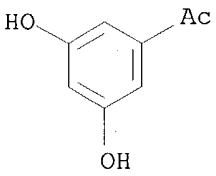
RN 4316-42-1 HCAPLUS
CN 1H-Imidazole, 1-butyl- (9CI) (CA INDEX NAME)



RN 36016-40-7 HCAPLUS
CN Hydroxylamine, O-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 51863-60-6 HCAPLUS
CN Ethanone, 1-(3,5-dihydroxyphenyl)- (9CI) (CA INDEX NAME)



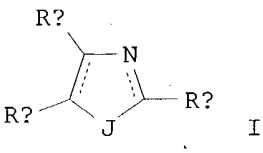
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:521487 HCAPLUS
DOCUMENT NUMBER: 137:93743
TITLE: Preparation of thiazole derivatives as **antiglaucoma** agents
INVENTOR(S): **Wagle, Dilip; Gall, Martin; Bell, Stanley C.; Lavoie, Edmond J.**
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002053156 | A1 | 20020711 | WO 2001-US49834 | 20011228 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1359910 | A1 | 20031112 | EP 2001-988373 | 20011228 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2002119970 | A1 | 20020829 | US 2001-36856 | 20011231 |

PRIORITY APPLN. INFO.: US 2000-259428P P 20001229
US 2001-296258P P 20010606
WO 2001-US49834 W 20011228
OTHER SOURCE(S): MARPAT 137:93743

GI



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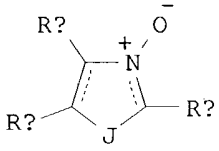


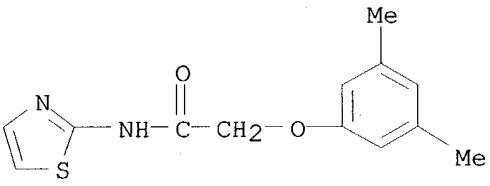
II

AB Provided is a method of decreasing intraocular pressure or improving ocular accommodation, comprising administration of I, II [J = O, S, NR'; Ra-b = H, acylamino, acyloxyalkyl, alkanoyl, alkenyl, alkoxy, etc.; R' = alkyl, alkenyl, H, Ar; Rc = oxo, H, alkyl, alkylthio, H, mercapto, amino, amino-alkyl, etc.]. For instance, 3,5-dimethylphenol was alkylated with bromoacetic acid (110°, 4 h) to yield (3,5-dimethylphenoxy)acetic acid which was coupled to 2-aminothiazole (CH2Cl2, EDCI, HOBt, NMM) to give 2-(3,5-Dimethylphenoxy)-N-(thiazol-2-yl)acetamide. The activity of example compds. in breaking, reversing or inhibiting the formation of advanced glycosylation end products (AGEs) or AGE-mediated cross-links was determined (no data).

IT **302559-76-8P**, 2-(3,5-Dimethylphenoxy)-N-(thiazol-2-yl)acetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**antiglaucoma** agent; preparation of thiazole derivs. as **antiglaucoma** agents)

RN 302559-76-8 HCAPLUS

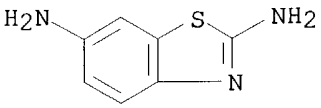
CN Acetamide, 2-(3,5-dimethylphenoxy)-N-2-thiazolyl- (9CI) (CA INDEX NAME)



IT **181070-25-7P**, 2,6-Diaminobenzothiazole dihydrochloride
**289491-05-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**antiglaucoma** agents; preparation of thiazole derivs. as **antiglaucoma** agents)

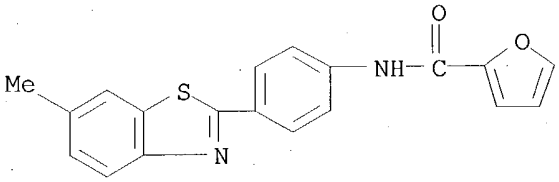
RN 181070-25-7 HCAPLUS

CN 2,6-Benzothiazolediamine, dihydrochloride (9CI) (CA INDEX NAME)



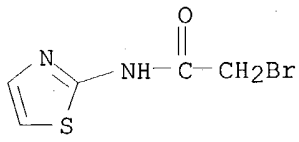
●2 HCl

RN 289491-05-0 HCAPLUS
CN 2-Furancarboxamide, N-[4-(6-methyl-2-benzothiazolyl)phenyl]- (9CI) (CA INDEX NAME)

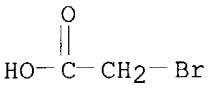


IT **9001-03-0**, Carbonic anhydrase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; preparation of thiazole derivs. as **antiglaucoma** agents)
RN 9001-03-0 HCAPLUS
CN Dehydratase, carbonate (9CI) (CA INDEX NAME)

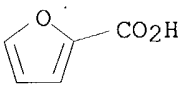
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **73326-20-2P**, 2-(2-Bromoacetamido)thiazole
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of thiazole derivs. as **antiglaucoma** agents)
RN 73326-20-2 HCAPLUS
CN Acetamide, 2-bromo-N-2-thiazolyl- (9CI) (CA INDEX NAME)



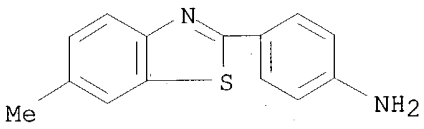
IT **79-08-3**, Bromoacetic acid **88-14-2**, 2-Furoic acid **92-36-4**, 2-(4-Aminophenyl)-6-methylbenzothiazole **96-50-4**, 2-Aminothiazole **108-68-9**, 3,5-Dimethylphenol **527-69-5**, 2-Furoyl chloride **598-21-0**, Bromoacetyl bromide **6285-57-0**, 2-Amino-6-nitrobenzothiazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of thiazole derivs. as **antiglaucoma** agents)
RN 79-08-3 HCAPLUS
CN Acetic acid, bromo- (8CI, 9CI) (CA INDEX NAME)



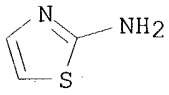
RN 88-14-2 HCAPLUS
CN 2-Furancarboxylic acid (9CI) (CA INDEX NAME)



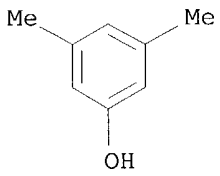
RN 92-36-4 HCAPLUS
CN Benzenamine, 4-(6-methyl-2-benzothiazolyl)- (9CI) (CA INDEX NAME)



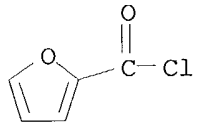
RN 96-50-4 HCAPLUS
CN 2-Thiazolamine (9CI) (CA INDEX NAME)



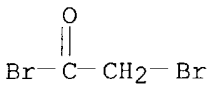
RN 108-68-9 HCAPLUS
CN Phenol, 3,5-dimethyl- (9CI) (CA INDEX NAME)



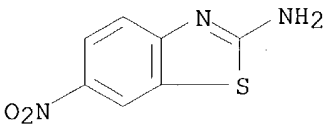
RN 527-69-5 HCAPLUS
CN 2-Furancarbonyl chloride (9CI) (CA INDEX NAME)



RN 598-21-0 HCAPLUS
CN Acetyl bromide, bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 6285-57-0 HCAPLUS
CN 2-Benzothiazolamine, 6-nitro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

-C.tplbond.CRE, -CH2-C.tplbond.CRP, aryl, arylalkyl, or aroylalkyl; R1 and R2 are independently hydrogen, alkyl or hydroxymethyl; R3 is H or -CH3; R4 is acetamido, hydrogen, Me, amino, -C.tplbond.CRE, -CH2-C.tplbond.CRP, alkylthio, fluoromethyl, etc.; X- is a pharmaceutically acceptable anion.

ACCESSION NUMBER: 2002:927189 HCAPLUS
DOCUMENT NUMBER: 138:11441
TITLE: Method for treating fibrotic diseases or other indications
INVENTOR(S): Gall, Martin
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002096362 | A2 | 20021205 | WO 2002-US16846 | 20020530 |
| WO 2002096362 | A3 | 20030522 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003004194 | A1 | 20030102 | US 2002-158344 | 20020530 |
| US 6596745 | B2 | 20030722 | | |
| EP 1404339 | A2 | 20040407 | EP 2002-739481 | 20020530 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |

PRIORITY APPLN. INFO.: US 2001-294438P P 20010530
WO 2002-US16846 W 20020530

OTHER SOURCE(S): MARPAT 138:11441

IT **Eye**, disease
(retinopathy; method for treating fibrotic diseases or other indications)

IT 477252-66-7P 477252-67-8P 477252-68-9P 477252-69-0P
**477252-70-3P 477252-71-4P 477252-72-5P**
**477252-73-6P** 477252-74-7P 477252-75-8P 477252-76-9P
477252-77-0P 477252-78-1P 477252-79-2P 477252-80-5P
**477252-81-6P 477252-82-7P 477252-83-8P**
**477252-84-9P** 477252-85-0P 477252-86-1P 477252-87-2DP, derivs.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for treating fibrotic diseases or other indications)

IT **477252-70-3P 477252-71-4P 477252-72-5P**
**477252-73-6P 477252-81-6P 477252-82-7P**
**477252-83-8P 477252-84-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES